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L3: Entry 6 of 7

File: USPT

DOCUMENT-IDENTIFIER: US 6362341 B1

TITLE: Benzyl compounds which inhibit leukocyte adhesion mediated by VLA-4

Detailed Description Text (34):

In addition, certain of the compounds of this invention inhibit, in vivo, adhesion of leukocytes to endothelial cells mediated by VLA-4 and, accordingly, can be used in the treatment of diseases mediated by VLA-4. Such diseases include inflammatory diseases in mammalian patients such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes (including acute juvenile onset diabetes), inflammatory bowel disease (including ulcerative colitis and Crohn's disease), multiple sclerosis, rheumatoid arthritis, tissue transplantation, tumor metastasis, meningitis, encephalitis, stroke, and other cerebral traumas, nephritis, retinitis, atopic dermatitis, psoriasis, myocardial ischemia and acute leukocyte-mediated lung injury such as that which occurs in adult respiratory distress syndrome.

Detailed Description Text (44):

The pharmaceutical compositions of the present invention can be used to block or inhibit cellular adhesion associated with a number of diseases and disorders. For instance, a number of inflammatory disorders are associated with integrins or leukocytes. Treatable disorders include, e.g., transplantation rejection (e.g., allograft rejection), Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes (including acute juvenile onset diabetes), retinitis, cancer metastases, rheumatoid arthritis, acute leukocyte-mediated lung injury (e.g., adult respiratory distress syndrome), asthma, nephritis, and acute and chronic inflammation, including atopic dermatitis, psoriasis, myocardial ischemia, and inflammatory bowel disease (including Crohn's disease and ulcerative colitis). In preferred embodiments, the pharmaceutical compositions are used to treat inflammatory brain disorders, such as multiple sclerosis (MS), viral meningitis and encephalitis.

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L8: Entry 44 of 54

File: USPT

DOCUMENT-IDENTIFIER: US 6190887 B1

TITLE: Expression of an exogenous gene in a mammalian cell by use of a non-mammalian DNA virus having an altered coat protein

Brief Summary Text (18):

In a preferred embodiment, the altered coat protein is produced as a fusion (i.e., chimeric) protein. A particularly useful fusion protein includes (i) a transmembrane polypeptide (e.g., antibodies such as IgM, IgG, and single chain antibodies) fused to (ii) a polypeptide that binds to a mammalian cell (e.g., VCAM, NCAM, integrins, and selectins) or to a growth factor. Included among the suitable transmembrane polypeptides are various coat proteins that naturally exist on the surface of a non-mammalian or mammalian virus particle (e.g., baculovirus gp64, influenza hemagglutinin protein, and Vesicular stomatitis virus glycoprotein G). All or a portion of the transmembrane polypeptide can be used, provided that the polypeptide spans the membrane of the virus particle, such that the polypeptide is anchored in the membrane. Non-viral transmembrane polypeptides also can be used. For example, a membrane-bound receptor can be fused to a polypeptide that binds a mammalian cell and used as the altered coat protein. Preferably, the fusion protein includes a viral coat protein (e.g., gp64) and a targeting molecule (e.g., VSV-G). Fusion polypeptides that include all or a cell-binding portion of a cell adhesion molecule also are included within the invention (e.g., a gp64-VCAM fusion protein).

Brief Summary Paragraph Table (3):

TABLE 2 EXAMPLES OF SUITABLE ALTERED COAT PROTEINS

Viral Coat Protein	Reference
Vesicular Stomatitis Virus glycoprotein G	GenBank Accession # M21416.sup.a
<u>Herpes Simplex Virus 1</u> (KOS) glycoprotein B	Accession # K01760
Human Immunodeficiency Virus type 1 gp120	Accession # U47783
Influenza A Virus hemagglutinin	GenBank Accession # M38242
Human Respiratory Syncytial Virus membrane glycoprotein	Accession # M86651
Human Respiratory Syncytial Virus fusion protein	Accession # D00334
Tick-Borne <u>Encephalitis Virus</u> glycoprotein E	Accession # S72426
Pseudorabies Virus glycoprotein gH	GenBank Accession # U11753
Rabies Virus G5803FX glycoprotein	GenBank Accession # M61196
Human Rhinovirus 1B viral coat proteins VP1, VP2, and VP3	Accession # D00239
Semliki Forest Virus coat proteins E1, E2, and E3	Accession # Z48163
Human immunodeficiency Virus-1 Mebatsion et al., 1996, PNAS envelope spike protein	93:11366-1370
<u>Herpes Simplex Virus-1</u> Entry Mediator	Montgomery et al., 1996, Cell 87:427-436
Pseudorabies Virus Glycoprotein gE	Enquist et al., 1994, J. Virol. 68:5275-5279
<u>Herpes Simplex Virus</u> Glycoprotein gB	Norais et al., 1996, J. Virol. 70:7379-7387
Bovine Syncytial Virus Envelope Protein	Renshaw et al., 1991, Gene 105:179-184
Human Foamy Virus (HFV) glycoprotein G	Gaudin et al., 1996, J. Virol. 70:7371-7378

sup.a The GenBank accession numbers refer to nucleic acid sequences encoding the viral coat proteins.

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<u>L11</u>	L9 and (encephalitis)	0	<u>L11</u>
<u>L10</u>	L9 and (alpha4 or 'vla-4')	0	<u>L10</u>
<u>L9</u>	rubin-steven\$	52	<u>L9</u>
<u>L8</u>	L6 and (adhesion or adhesive) and ('alpha4' or 'vla-4' or vcam\$)	54	<u>L8</u>
<u>L7</u>	L6 and (adhesion or adhesive)	219	<u>L7</u>
<u>L6</u>	(herpes or arbovirus) same (encephalitis)	1152	<u>L6</u>

DB=JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ

<u>L5</u>	(alpha4 or 'vla-4')and (viral or virus or herpes or arbovirus) same (encephalitis)	5	<u>L5</u>
<u>L4</u>	L1 and (viral or virus or herpes or arbovirus) same (encephalitis)	0	<u>L4</u>

DB=USPT,PGPB; PLUR=YES; OP=ADJ

<u>L3</u>	L1 and (viral or virus or herpes or arbovirus) same (encephalitis)	7	<u>L3</u>
<u>L2</u>	L1 same (viral or virus or herpes or arbovirus)	0	<u>L2</u>
<u>L1</u>	('vla-4' or alpha4) same (encephalitis)	20	<u>L1</u>

END OF SEARCH HISTORY